



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Dated: January 27, 2003

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Serial No. : 09/768,661 Examiner Christopher J. Nicols, Ph.D.

Filed : January 23, 2001 Group Art Unit 1647

For : CELL-SIGNALING ASSAYS

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Commissioner for Patents
Washington, D.C. 20231

FEB 05 2003

TECH CENTER 1600/2900

Sir:

AMENDMENT

Responsive to the Office action dated August 26, 2002, applicants hereby amend the above-identified patent application as follows:

In the claims:

Please cancel claims 1-35, without prejudice.

Please add new claims 36-57, as follows:

36. A method of identifying a compound as a modulator of a reaction that generates or consumes a cyclic nucleotide, comprising:

conducting the reaction that generates or consumes a cyclic nucleotide in the presence of a candidate compound;

contacting a product of the reaction with a luminescent tracer and with the opposite member of a specific binding pair to the cyclic nucleotide, wherein the tracer and the cyclic nucleotide compete for binding to the opposite member of the specific binding pair;

illuminating the tracer with polarized light, wherein the light is capable of inducing emission of polarized light from the tracer;
detecting the extent of polarization of light emitted from the tracer; and
identifying the candidate compound as a modulator of the reaction based on the extent of polarization of the emitted light.

37. The method of claim 36, wherein the cyclic nucleotide is selected from the group consisting of cAMP and cGMP.

38. The method of claim 36, wherein the opposite member of a specific binding pair is an immunological binding partner.

39. The method of claim 36, wherein the extent of polarization is determined using a function selected from the group consisting of polarization and anisotropy.

40. The method of claim 36, wherein the extent of polarization of the emitted light is inversely correlated with the concentration of the cyclic nucleotide.

41. The method of claim 36, further comprising determining the concentration of the cyclic nucleotide.

42. The method of claim 36, wherein the reaction is conducted using whole cells.

43. The method of claim 36, wherein the reaction is conducted using lysed cells.

44. The method of claim 36, wherein the reaction generates a cyclic nucleotide.

45. The method of claim 44, wherein the reaction is catalyzed by a cyclase.

46. The method of claim 36, wherein the reaction consumes a cyclic nucleotide.

47. The method of claim 46, wherein the reaction is catalyzed by a phosphodiesterase.

48. The method of claim 36, further comprising repeating the steps of conducting, contacting, illuminating, and measuring in the absence of a candidate compound, wherein the step of identifying the candidate compound as a modulator includes comparing the extent of polarization of the emitted light based on the reaction conducted in the presence of the candidate compound to the extent of polarization of the emitted light based on the reaction conducted in the absence of the candidate compound.

49. The method of claim 48, the reaction generating a cyclic nucleotide, wherein an increase in the extent of polarization when the reaction is conducted in the presence of the candidate compound in comparison with the extent of polarization when the reaction is conducted in the absence of the candidate compound identifies the candidate compound as an inhibitor of the reaction, and wherein a decrease in the extent of polarization when the reaction is conducted in the presence of the candidate compound in comparison with the extent when the reaction is conducted in the absence of the candidate compound identifies the candidate compound as an agonist of the reaction.

50. The method of claim 48, the reaction consuming a cyclic nucleotide, wherein an increase in the extent of polarization when the reaction is conducted in the presence of the candidate compound in comparison with the extent of polarization when the reaction is conducted in the absence of the candidate compound identifies the candidate compound as an agonist of the reaction, and wherein a decrease in the extent of polarization when the reaction is conducted in the presence of the candidate compound in comparison with the extent when the reaction is conducted in the absence of the candidate compound identifies the candidate compound as an inhibitor of the reaction.

51. The method of claim 36, the reaction generating a cyclic nucleotide, wherein the step of conducting the reaction includes providing a nucleotide triphosphate.

52. The method of claim 36, the reaction consuming a cyclic nucleotide, wherein the step of conducting the reaction includes providing the cyclic nucleotide.

53. The method of claim 36, further comprising repeating the steps of conducting, contacting, illuminating, measuring, and identifying for a different candidate compound.

54. The method of claim 53, at least one of the steps being performed using a microplate, wherein a different well of the microplate is used for each different candidate compound.

55. The method of claim 36, wherein at least one of the steps of conducting, contacting, illuminating, measuring, and identifying is performed using a microplate.

56. The method of claim 36, the step of conducting the reaction being performed in a reaction volume, wherein the step of contacting includes adding the luminescent tracer and the opposite member of a specific binding pair to the reaction volume.

57. The method of claim 36, wherein the luminescent tracer comprises a cyclic nucleotide coupled to a luminophore.